# Potential Issues Related to the Ethical Basis for the Oversight and Actions of Institutional Review Boards in Relation to EPA's Proposed Rule "Strengthening Transparency in Regulatory Science"

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Dear Dr. Armitage:

Thank you for the opportunity to provide my comments to the EPA Scientific Advisory Board (SAB) concerning its January 17, 2020, meeting on "SAB Consideration of the Scientific and Technical Basis of EPA's Proposed Rule Titled Strengthening Transparency in Regulatory Science."

I am a physician and environmental health scientist, and a former EPA Assistant Administrator for Research and Development under Administrators Ruckelshaus and Thomas. My background as a physician includes board certification in Internal Medicine and Hematology. My clinical research was recognized through election to the American Society of Clinical Investigation, and my total research career through election to the National Academy of Medicine. Through my career, I have had frequent direct interaction with Institutional Review Boards, including the still- fresh memory of having a proposal rejected by the NYU Medical School's IRB a half century ago. More recently, as a director of a program with an active environmental epidemiology unit, and then Dean of the University of Pittsburgh Graduate School of Public Health for a period during which I estimate we had over $200 million of funded human research, my involvement in discussions with IRBs has broadened and deepened.

I presented oral comments at the previous meeting of the Science Advisory Board considering the issue of the Scientific and Technical Basis of EPA's Proposed Rule Titled "Strengthening Transparency in Regulatory Science." Among the issues I raised was the very strong possibility that Institutional Review Boards (IRBs) would require their approval before any unpublished information about the study could be turned over to EPA, and that to do so they would need to consider a number of ethical issues that I had not seen reflected in the various documents. I note that in their individual comments following this meeting, a number of the SAB members have raised the issue of the role of the IRBs. Further, the draft SAB report makes the important distinction between issues posed by large data sets currently used for governmental purposes, e.g., census data, and the data sets developed and used by academics and individual societies.

Since my earlier presentation to the SAB, I have taken the opportunity to individually sample the opinion of a few individual scientists or ethicists with IRB experience at major academic health institutions. This small sample was unanimous in saying that the original IRB would need to give its approval before investigators could turn over unpublished information that was part of the previously approved study. They also thought that the issue of equipoise which I previously raised was of significance, but cautioned that individual IRBs might interpret this differently depending

upon the circumstances, particularly as they were unaware of it having been considered before in this context.

Institutional Review Boards' use of ethical concepts as a basis to decide on the appropriateness of human research studies has evolved through recent decades. There have been many meetings on the subject, and a number of National Academy of Sciences (NAS) committees have considered the ethical constraints related to the release of data. These ethical constraints are central to decisions as to whether to approve and how to perform research, and presumably would apply to decisions related to turning unpublished data over to a third party for potential public availability.

One of the ethical concepts used by IRBs in approving studies is that of "equipoise," which is often defined as requiring a state of genuine uncertainty, and the lack of likely bias in the outcome of the study. The equipoise issue might well be used by an IRB to refuse to allow investigators to hand over raw data to EPA. Although sometimes controversial, many IRBs interpret their mandate as including whether the proposed study is scientifically valid. If not, there would then be no ethical basis on which to expose humans to any risk – including having their personal information at risk of disclosure. Central to the issues posed by EPA's proposed transparency rule is that an IRB could also turn down release of information that they judge would likely be used in ways that were inherently biased.

Based upon the principle of equipoise, the IRB would perhaps have three grounds to oppose turning over the data to EPA in such a way that it could be given to virtually anyone who requested it. One is the degree of certainty, based upon past behavior by industry in similar situations, that a regulated industry would hire consultants whose future success depended on finding and exaggerating minor potential confounding factors suggested by the raw data. Raising the possibility of an unmeasurable confounder is relatively easy in any study that cannot be done in a random double-blind fashion – which is true for virtually all environmental health studies. (See my previous SAB presentation on the inability of most human environmental health research to conform to the gold standard of a randomized double blind study, and let me emphasize that not all consultants bias their science because of their desire to be rehired by their clients). In other words, the already existing evidence that such disclosure leads to a biased study could be construed as grounds for the IRB to refuse permission.

Another ground for refusal is that IRBs have problems approving studies that cannot fulfill their stated aim, which EPA claims if for replication. In environmental health, reanalysis of the same data is not the usual pathway to replication. In environmental health, replication is generally achieved by multiple studies by different investigators on different populations using different scientific approaches.

A third potentially pertinent argument, and perhaps the most powerful to an IRB, is that release of the unpublished data has a strong potential for bias in that only industry could afford to hire consultants to reanalyze the data, while community groups could not. This would be particularly true of groups from disadvantaged communities, and therefore release of the data would contribute to environmental justice concerns. Similarly, equipoise is unlikely to be achieved when it appears that

EPA has a regulatory preference that can be construed by IRB members to impact on the reinterpretation of the study data.

In essence, I am arguing that an IRB's equipoise-based argument not to allow release of information on a published study uses reasoning that is far stronger than that used by the current EPA leadership in excluding EPA-funded scientists, usually academics, from serving on an EPA advisory committee. The difference, of course, is that the checks and balances in academia that guard against an EPA-funded academic scientist intentionally distorting science to favor EPA are infinitely greater than that used by industries looking for consultants to support their profit-making enterprises. An academic scientist suspected by his or her peers of getting the science wrong will have trouble with their careers. It is peers who will review their manuscripts for publication, serve on study sections who decide whether their grant proposal will be competitively funded, and whose opinion will be sought by the Provost's office for decisions about promotion. In contrast, it can much more readily be argued that consultants who can use shaky science to provide ammunition for those who hire them likely will be rehired. Accordingly, EPA's arguments on which they base the exclusion of EPA-funded academic scientists from giving EPA advice could easily be used by an IRB to exclude release of unpublished data to EPA.

In my earlier presentation to the SAB, I emphasized that while knowledgeable about IRBs, I was not an expert on this subject. But, as I pointed out, this is also true for the SAB members. With an ethical issue of this importance facing EPA, it is unconscionable for EPA not to ask for a thorough review of this issue, preferably by the NAS who has taken the lead in this area. This would include a workshop soliciting public input and a full committee report.

With apologies to Admiral Farragut, EPA should avoid being seen as saying "Damn the ethics, full speed ahead."

Sincerely yours,

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